

#### Rejections Under 35 U.S.C. § 112, first paragraph

The Examiner has maintained the rejection under 35 U.S.C. § 112, first paragraph based upon the contended lack of deposit of the recited cell lines. Upon indication of allowable subject matter herein, applicants will make any required deposits in accordance with 37 C.F.R. §1.803.

#### Rejections Based On Double Patenting

The Examiner has rejected claim 1, contending that the claim is unpatentable over claim 7 of U.S. Patent No. 6,361,771 B1 (“the ‘771 patent”). The Examiner has indicated that a showing that the conflicting inventions are commonly owned will obviate this rejection. Accordingly, applicants have attached hereto Appendix B which is a the cover page for United States Patent Application Serial Number 6,361,771 and Appendix C which is a copy of the Assignment recorded in the pending application. Applicants note that both the ‘771 patent and the pending application are owned by Neurotech S.A. In addition, applicants stand ready to file a terminal disclaimer upon indication that the claims are in condition for Allowance.

#### Rejections Under 35 U.S.C. § 102(e)

Claims 1 and 24 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,361,771 B1 (“the ‘771 patent”). Specifically, the Examiner contends that the ‘771 patent teaches “ARPE-19 comprising an expression vector coding for” various polypeptides. Applicants have filed herewith a declaration under Rule 1.131 demonstrating that the date of invention by the inventor Weng Tao precedes the filing date of the ‘771 patent. Accordingly, applicants respectfully request that the rejection be withdrawn.

CONCLUSION

Applicants believe that the claims, as amended are in condition for allowance. If the Examiner has any questions, the Examiner is invited to contact the undersigned by telephone.

Respectfully submitted,

Dated: March 14, 2003

Scott Miller  
Ivor R. Elrifi, Reg. No. 39,529  
Scott D. Miller, Reg. No. 43,803  
Attorneys for Applicants  
MINTZ, LEVIN COHN FERRIS  
GLOVSKY & POPEO P.C.  
Chrysler Center  
666 Third Avenue, 24<sup>th</sup> Floor  
New York, New York 10017  
Tel: (212) 935-3000  
Fax: (212) 983-3155



35437

PATENT TRADEMARK OFFICE

## APPENDIX A

### Claim Amendments in Bracket and Underline Form

24. (Three Times Amended) A method of producing a therapeutic polypeptide to treat primary or secondary ophthalmologic or neurological disorders, comprising incubating [cells of] a mammalian retinal pigment epithelial cell line wherein the cell line is selected from the group comprising hRPE-7, hRPE-116 and ARPE-19 in a biological compatible medium such that the cell line produces the polypeptide and wherein [the cells of] the cell line comprises an expression vector comprising a polynucleotide coding for a polypeptide selected from the group comprising BDNF, NT-4, CNTF, Axokine, FGF-2 (bFGF), IGF I, IGF II, TGF $\beta$ -II, Midkine, IL-1 $\beta$ , TNF, NGF, IL-2/3, ILF, IL-6, NTN, Neublastin, VEGF, GDNF, PDGF, LEDGF and PEDF.
37. (Three Times Amended) The cell line IO/JG2/1, deposited under I-1695 on April 18, 1996 in the Collection Nationale de Cultures de Micro-organismes held by the [Insititute] Institut Pasteur, Paris France.

NYC 256554v1



US006361771B1

(12) **United States Patent**  
**Tao et al.**(10) **Patent No.:** **US 6,361,771 B1**  
(45) **Date of Patent:** **Mar. 26, 2002**(54) **ARPE-19 AS A PLATFORM CELL LINE FOR  
ENCAPSULATED CELL-BASED DELIVERY**(75) **Inventors:** **Weng Tao**, Lincon, RI (US); **David H. Rein**, Cambridge, MA (US); **Brenda J. Dean**, Cumberland, RI (US); **Paul F. Stabila**, Coventry, RI (US); **Moses B.I. Goddard**, Tiverton, RI (US)(73) **Assignee:** **Neurotech S.A.**, Evry (FR)( \* ) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.(21) **Appl. No.:** **09/543,119**(22) **Filed:** **Apr. 5, 2000****Related U.S. Application Data**

(60) Provisional application No. 60/127,926, filed on Apr. 6, 1999.

(51) **Int. Cl.<sup>7</sup>** ..... **A61K 48/00**; **A61K 9/22**;  
**C12N 15/163**; **C12N 5/108**; **A61M 3/00**(52) **U.S. Cl.** ..... **424/93.21**; **435/320.1**;  
**435/325**; **435/455**; **435/366**; **435/371**; **604/890.1**;  
**604/43**; **604/93**(58) **Field of Search** ..... **424/93.21**, **93.2**,  
**424/93.1**; **514/44**; **435/325**, **455**, **320.1**,  
**366**, **371**; **604/890.1**, **44**, **93**, **27**, **174**, **175**(56) **References Cited****U.S. PATENT DOCUMENTS**

4,892,538 A	1/1990	Aebischer et al.	604/891.1
4,968,733 A	11/1990	Müller et al.	521/64
4,976,859 A	12/1990	Wechs	210/500.23
5,106,627 A	4/1992	Aebischer et al.	424/424
5,156,844 A	10/1992	Aebischer et al.	424/424
5,158,881 A	10/1992	Aebischer et al.	435/182
5,283,187 A	2/1994	Aebischer et al.	435/185
5,284,761 A	2/1994	Aebischer et al.	435/182
5,512,600 A	4/1996	Mikos et al.	521/61
5,550,050 A	8/1996	Holland et al.	435/240.2
5,554,148 A	9/1996	Aebischer et al.	604/890
5,614,404 A	3/1997	Mazzara et al.	435/236
5,639,275 A	6/1997	Baetge et al.	604/891
5,641,750 A *	6/1997	Louis	514/12
5,653,687 A	8/1997	Mills et al.	604/57
5,653,975 A	8/1997	Baetge et al.	424/93.1

5,904,144 A \* 5/1999 Hammang et al. .... 128/898  
6,020,192 A \* 2/2000 Muzyczka et al. .... 435/320.1**FOREIGN PATENT DOCUMENTS**

WO	WO 92/19195	11/1992
WO	WO 93/06222	4/1993
WO	WO 94/01139	1/1994
WO	WO 95/05452	2/1995
WO	WO 97/34586	9/1997
WO	WO 97/44065	11/1997
WO	WO 98/05304	2/1998
WO	WO 99/52573	10/1999

**OTHER PUBLICATIONS**

Wivel, N.A. & Wilson, J. M. Hematol. Oncol. Clin. North Am. 12:483-501, 1998.\*  
 Dunn et al. Exp. Eye Res. 62:155-169, 1996.\*  
 Aebischer et al. Nat. Med. 2:696-699, 1996.\*  
 Cayouette et al. J. Neurosci. 18:9282-9293, 1998.\*  
 American Type Culture Collection Web page <http://phage.atcc.org> (ATCC No. CRL-2302).  
 Dunn et al., 39 Invest. Ophthalmol. Vis. Sci. 2744-9 (1998).  
 Emerich et al., 16 J. Neurosci. 5168-81 (1996).  
 Finnemann et al., 94 Proc. Natl. Acad. Sci. USA 12932-7 (1997).  
 Handa et al., 66 Exp. Eye. 411-9 (1998).  
 Holtkamp et al., 112 Clin. Exp. Immunol. 34-43 (1998).  
 Maidji et al., 70 J. Virol. 8402-10 (1996).

\* cited by examiner

*Primary Examiner*—Dave T. Nguyen*Assistant Examiner*—Quang Nguyen(74) *Attorney, Agent, or Firm*—Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, PC; Ivor R. Elrifi, Esq.; Christina V. Karnakis, Esq.(57) **ABSTRACT**

ARPE-19 cells were evaluated as a platform cell line for encapsulated and un-encapsulated cell-based delivery technology. ARPE-19 cells were found to be hardy (the cell line is viable under stringent conditions, such as in central nervous system or intra-ocular environment); can be genetically modified to secrete the protein of choice; has a long life span; is of human origin; has good in vivo device viability; delivers efficacious quantity of growth factor; triggers no or low level host immune reaction, and is non-tumorigenic.

**14 Claims, 2 Drawing Sheets**

## ASSIGNMENT

We, **John Greenwood, Peter Adamson, and Raymond Lund**, the undersigned, for good and valuable consideration, the receipt of which is hereby acknowledged, hereby assign, sell and transfer to **NEUROTECH S.A.**, a French corporation, with offices at **Bâtiment Génopole-Industries, 4, rue Pierre Fontaine, 91000 EVRY, FRANCE**, and its successors, assigns and legal representatives, all hereinafter referred to as the ASSIGNEE: (1) our entire right, title and interest for the United States and in all countries, in and to any and all inventions, discoveries and applications which are disclosed in the application for United States Letters Patent entitled:

### **RETINAL CELL LINES WITH EXTENDED LIFE-SPAN AND THEIR APPLICATIONS**

filed with the U.S. Patent and Trademark Office on **April 27, 2000** and assigned Serial No. **09/559,707**, including any renewals, revivals, reissues, reexaminations, extensions, continuations and divisions thereof and any substitute applications therefor; (2) the full and complete right to file patent applications in the name of the ASSIGNEE, its designee, or in our names at the ASSIGNEE, or its designee's election, on the aforesaid inventions, discoveries and applications in all countries of the world; (3) the entire right, title and interest in and to any Letters Patent which may issue thereon in the United States or in any country, and any renewals, revivals, reissues, reexaminations and extensions thereof, and any patents of confirmation, registration and importation of the same; and (4) the entire right, title and interest in all Convention and Treaty Rights of all kinds thereon, including without limitation all rights of priority in any country of the world, in and to the above inventions, discoveries and applications.

We hereby authorize and request the competent authorities to grant and to issue any and all such Letters Patent in the United States and throughout the world to the ASSIGNEE of the entire right, title and interest therein, as fully and entirely as the same would have been held and enjoyed by me/us had this assignment, sale and transfer not been made.

We agree, at any time, upon the request of the ASSIGNEE, to execute and to deliver to the ASSIGNEE any additional applications for patents for said inventions and discoveries, or any part or parts thereof, and any applications for patents of confirmation, registration and importation based on any Letters Patent issuing on said inventions, discoveries, or applications and divisions, continuations, renewals, revivals, reissues, reexaminations and extensions thereof.

We further agree at any time to execute and to deliver upon request of the ASSIGNEE such additional documents, if any, as are necessary or desirable to secure patent protection on said inventions, discoveries and applications throughout all countries of the world, and otherwise to do the necessary to give full effect to and to perfect the rights of the ASSIGNEE under this Assignment, including the execution, delivery and procurement of any and all further documents evidencing this assignment, transfer and sale as may be necessary or desirable.

APPLICANTS: Greenwood et al.  
SAL NUMBER: 09/559,707

hereby covenant that no assignment, sale, agreement or encumbrance has been or will be made entered into which would conflict with this assignment.

further covenant that ASSIGNEE will, upon its request, be provided promptly with all pertinent papers and documents relating to said invention and said Letters Patent and legal equivalents as may be known and accessible to ASSIGNOR and will testify as to the same in any interference, litigation or proceeding related thereto and will promptly execute and deliver to ASSIGNEE or its legal representatives any and all papers, instruments or affidavits required to apply for, obtain, maintain, issue and enforce said application, said invention and said Letters Patent and said legal equivalents thereof which may be necessary or desirable to carry out the purposes thereof.

etc:

16/11/00

Signature of: John Greenwood

IN WITNESS WHEREOF, We have hereunto set hand and seal

Clare Walters CLARE WALTERS  
Signature of witness:

this 16 day of NOV 2000  
Date of signing

Date:

16 Nov 2000

Signature of: Peter Adamson

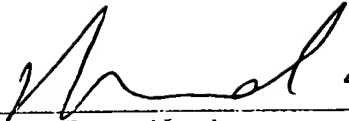
IN WITNESS WHEREOF, We have hereunto set hand and seal

Clare Walters CLARE WALTERS  
Signature of witness:

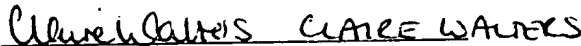
this 16 day of NOV. 2000  
Date of signing

APPLICANTS: Greenwood et al  
SERIAL NUMBER: 09/559,787

Date:

  
Signature of: Raymond Lund

IN WITNESS WHEREOF, We have hereunto set hand and seal

  
Signature of witness:

this 16 day of NOV. 2000  
Date of signing

TRADOC:1157145.1(T362011.DOC)  
08/11/00 10:32 AM

10:0 0160878950 NEUROTECH

N2.5004 10.10.00 10:1